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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAMBERTSON, DAVID A	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,471	KHODADOUST, MEHRAN M.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61 and 63-82* is/are pending in the application.

4a) Of the above claim(s) *1-52 and 69-78* is/are withdrawn from consideration.

5)☒ Claim(s) *54,55 and 61* is/are allowed.

6)☒ Claim(s) *53,56,57,59,60,63-68 and 79-82* is/are rejected.

7)☒ Claim(s) *58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed October 6, 2004. Amendments were made to the claims. Specifically, new claims 79-82 were added, and claim 62 was cancelled.

Claims 1-61 and 63-82 are pending in the instant application. Claims 1-52 and 69-78 are withdrawn from consideration as being drawn to a non-elected invention. Claims 53-61, 63-68 and 79-82 are currently under examination. Any rejection of record in the previous Office Action, mailed April 8, 2004, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

This application contains claims 1-52 and 69-78 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

New Rejections, Necessitated by Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following rejections are based on the following interpretation of the term "reporter." Absent an explicit definition to the contrary, a "reporter" is any polypeptide sequence (as encoded by a polynucleotide sequence) that can be detected by conventional means. This includes colorimetric assays, bio- or chemiluminescence assays, as well as screening assays such as selection on a particular growth medium (such as a positive or negative selection marker). Because any polypeptide sequence can be detected by some means (e.g., by measuring its enzymatic activity, or detecting it with specific antibodies), any polypeptide meets the limitation of being a "reporter."

Claims 53, 56, 59, 63-67 and 79-82 are rejected under 35 U.S.C. 102(b) as being anticipated by Baetscher *et al.* (US 5,922,601; see entire document; henceforth Baetscher). **This is a new rejection that is necessitated by the amendment of the claims.**

Baetscher teaches a nucleic acid construct comprising the following elements in a 5'-to-3' orientation:

Splice acceptor---IRES---Neo-HSV-TK (see for example Figure 2).

Because the Neomycin resistance gene is a positive selection marker (as set forth in dependent claim 80) and HSV-TK is a negative selection marker (as set forth in dependent claim 79), the above specific construct teaches the following general formula:

Splice acceptor---IRES---positive selection---negative selection.

This nucleic acid construct is then placed within the context of a retroviral vector construct (see for example column 12, lines 34-55), which along with LTR elements (i.e., integration sequences) additionally contains selectable or assayable markers, including those

useful in "fluorescence activated cell sorting" (see for example column 8, lines 50-57). Thus, the general formula of the nucleic acid construct taught by Baetscher has the overall general formula of:

Splice acceptor---IRES---positive selection---negative selection---reporter. This general construct anticipates claim 53.

Specifically, in order to get proper translation of the positive/negative selection marker, a translation stop codon must be present at the end of the coding sequence. Indeed, Baetscher also anticipates adding a Stop codon downstream from the selectable markers (see for example column 5, lines 22-29). Furthermore, in order to get expression of the reporter, a promoter element must be operatively linked to the reporter gene. Thus, the construct taught by Baetscher can further be visualized as having the following general formula:

Splice acceptor---IRES---positive selection---negative selection---STOP---Promoter---reporter. This construct anticipates claim 56.

Importantly, as set forth above, the retroviral vector further comprises selectable or assayable markers, including those useful in "fluorescence activated cell sorting" (see for example column 8, lines 50-57). Such a reporter can be a "protein that spontaneously emits light...Green Fluorescent Protein (GFP)" (see for example column 10, lines 12-19), which anticipates both claims 81 and 82.

Notably, the Neo-HSV-Tk marker is not operably linked to a promoter within the context of the nucleotide construct; i.e., it is a promoterless marker construct (see for example column 5, lines 44-67). As a result, the selection markers are only expressed when the construct integrates into the genome of a host cell, and the selection markers become operably linked to an

endogenous promoter element of the host cell (see for example column 13, lines 25-33). Thus, Baetscher also teaches a host cell comprising the claimed nucleic acid constructs/vectors.

Finally, Baetscher teaches a particular vector having the following formula:

Splice acceptor---IRES---Neo-HSV-TK---STOP---Promoter---Ampicillin. This vector anticipates claim 59.

Support for such a vector comes both from the above analysis of the teachings, and from column 12, lines 63-67, which indicate that the retroviral vector of the element can contain "regulatory elements suitable for propagation and selection in *E. coli*." This includes the Ampicillin resistance gene, which can serve as a positive selection marker (in the presence of ampicillin), and a prokaryotic promoter (i.e., regulatory element) to allow the expression of the Ampicillin resistance gene. Furthermore, given the interpretation of a reporter molecule set forth above, the Neomycin resistance gene can also be a reporter, allowing for the following formula:

Splice acceptor---IRES---reporter---negative marker---STOP---Promoter---positive marker,

which is a particular embodiment of claim 59.

In conclusion, Baetscher meets all of the limitations of the above indicated claims as amended, and therefore anticipates the claimed invention.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 53, 57, 60, 63, 65-67 and 79-82 are rejected under 35 U.S.C. 102(e) as being anticipated by Tessier-Lavigne *et al.* (US 6,248,934; see entire document; henceforth Tessier). **This is a new rejection that is necessitated by the amendment of the claims.**

Tessier teaches a nucleic acid construct comprising the following elements in a 5'-to-3' orientation:

Splice Acceptor---β-galactosidase---Neomycin---IRES---PLAP (see for example figure 1(a).

It is important to note that β-galactosidase is an enzymatic reporter protein (as indicated in dependent claims 81 and 82), and that the Neomycin resistance gene is a positive selection marker (as indicated in dependent claim 80). Furthermore, both markers are promoterless within the context of the construct, and can only be expressed upon integration (meaning the construct must contain integration sequences) into the genome of a host cell (see for example column 3, line 60 to column 4, line 14), when they become operably linked to an endogenous promoter. Thus, Tessier anticipates the following generic formula:

Splice Acceptor---reporter---positive marker---IRES---reporter. This anticipates claim 53.

Tessier also teaches that PLAP (i.e., the reporter) can be substituted for a negative selection marker, such as diptheria toxin (as indicated in dependent claim 79) (see for example column 4, lines 59-65). Tessier further teaches that this construct can contain a transcription factor (i.e., transactivator polypeptide) coding sequence (see for example column 4, lines 33-59). Thus, Tessier also teaches the general formula:

Splice Acceptor---reporter---positive marker---IRES---negative marker---transactivator polypeptide. This anticipates both claims 57 and 60.

Finally, Tessier teaches vectors comprising these nucleic acid constructs, as well as host cells that comprise said vectors (see for example column 2, lines 24-37).. As such, Tessier teaches all of the limitations of the aforementioned claims, thereby anticipating the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 53, 56, 57, 59, 60, 63, 65-67, 79-82 and 64* are rejected under 35 U.S.C. 103(a) as being unpatentable over Tessier in view of Baetscher, both as recited above. (Note: * denotes the claim that is newly rejected by the combination of references). **This is a new rejection that is necessitated by the amendment of the claims.**

Tessier teaches each of the elements set forth above in the rejection of claims 53, 57, 60, 63, 65-67 and 79-82 under 35 U.S.C. 102(e). Briefly, Tessier teaches the construction of nucleic acids to be used as gene trap vectors that can integrate into the genome of a eukaryotic host cell. However, although Tessier does teach the use of vectors, generically, there is no specific indication to use a retroviral vector.

Baetscher teaches each of the elements set forth above in the rejection of claims 53, 56, 59, 63-67 and 79-82 under 35 U.S.C. 102(b). Briefly, Baetscher also teaches the construction of nucleic acids to be used as gene trap vectors that can integrate into the genome of a host cell. Baetscher further indicates that retroviral vectors are useful for the efficient delivery of the nucleic acid constructs into eukaryotic cells (see for example column 12, lines 34-37).

It would have been obvious to combine the teachings of Tessier and Baetscher because the teachings all relate to the construction of gene trap vectors for integration into the genomes of eukaryotic host cells, thus the inventions are related in analogous (almost identical) technical fields. The ordinary skilled artisan would have been motivated to construct a retroviral vector comprising the nucleic acid taught specifically by Tessier because Tessier teaches the use of vectors, broadly, and Baetscher teaches that the use of retroviral vectors are useful for the efficient delivery of the nucleic acid constructs into eukaryotic cells. Thus, the skilled artisan would place the nucleic acids of Tessier into retroviral vectors to increase the efficiency of their integration into their target host cell genomes. Absent evidence to the contrary, the skilled ordinary skilled artisan would have had a reasonable expectation of success when combining the teachings of Tessier and Baetscher.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 68 is rejected under 35 U.S.C. 102(b) as being anticipated by Brent et al (US 5,695,941, as cited in the previous Office Action). **This rejection is maintained for reasons set forth in the previous Office Action.**

Response to Arguments Concerning Claim Rejections - 35 USC § 102

Applicant's arguments filed October 6, 2004 have been fully considered but they are not persuasive. Applicant's provided the following arguments concerning the rejection of claim 68:

It is asserted that Brent does not disclose a transactivator polypeptide as a limitation of the claims. Specifically, it is stated that the bait proteins cannot act as transactivators because "*the bait protein lacks its own activation domain*" (Applicant's emphasis). Applicant suggests that the Examiner has erroneously characterized the teachings of Brent because "Transactivation...results from the action of two individual polypeptides: one containing the bait protein...and the other containing the activation domain and the prey protein" (Applicant's emphasis)(see pages 31-32, the bridging paragraph of Applicant's response).

Applicant's argument is not found convincing because Applicant does not consider the definition of "transactivator polypeptide" as set forth in the instant specification (see for example page 34). In this section, a "transactivator" and a "transactivator polypeptide" are defined as "nucleic acid sequences and polypeptides, respectively, that transcribes, or causes the transcription of a protein which effects the regulation of a genomic loci..." and "[T]he transactivator polypeptides may directly or *indirectly* activate the transcription of a gene" (emphasis added). Nothing in this definition indicates that the "transactivator polypeptide" must

be a single polypeptide, or that it cannot be two separate polypeptides. Indeed, the statement that a "transactivator" may affect transcription "indirectly" includes the potential for the transactivator to act as two individual polypeptides. In this sense, a chimeric bait protein lacking its activation domain, but which can interact with a second polypeptide that contains an appropriate activation domain thereby activating transcription, is a clear example of "indirectly" activating transcription. Because Applicant's definition of the term "transactivator polypeptide" allows for such indirect activation, it is maintained that Brent indeed teaches the presence of a transactivator polypeptide. As such, the rejection of claim 68 as anticipated by Brent is maintained.

Allowable Subject Matter

Claims 54, 55 and 61 are allowed.

Claim 58 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
AU 1636

JAMES KETTER
PRIMARY EXAMINER